Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. *(currently amended)* An isolated anti-angiogenic ~~polypeptide or~~ peptide that is ~~selected from the group consisting of~~:

~~(a) a conservative amino acid substitution variant of SEQ ID NO:5 or SEQ ID NO:6 having substantially the same transition metal ion- or plasminogen- binding activity or substantially the same biologic activity as a polypeptide of the sequence SEQ ID NO:5 or SEQ ID NO:6; and~~

(a[[b]]) a pentapeptide, ~~consensus subsequence from SEQ ID NO:5 or 6 consisting of (i)~~ the sequence of which is (His,Pro)-(His,Pro)-Pro-His-Gly (SEQ ID NO:7), or

(b[[ii]]) an addition variant thereof ~~of SEQ ID NO:7 to~~ in which 1 to 4 amino acids selected from His, Pro and Gly are added [[at]] to the N- or C-terminus of SEQ ID NO:7, ~~1 to 4 amino acids selected from His, Pro and Gly~~,

wherein the ~~which penta~~peptide ~~or addition variant~~ has substantially the same transition metal ion- or plasminogen- binding activity or substantially the same biologic activity as (i) human HPRG, (ii) rabbit HPRG, or ~~as~~ (iii) a polypeptide domain of human or rabbit HPRG the sequence of which is SEQ ID NO:5 or SEQ ID NO:6, which biological activity ~~in (a) or (b)~~ is that of inhibiting (i) angiogenesis, (ii) endothelial cell proliferation or (iii) endothelial tube formation in an *in vitro* or *in vivo* bioassay.

2. *(currently amended)* The isolated peptide of claim 1 which is

(i) said pentapeptide ~~of (b) with a~~ wherein the sequence is selected from the group consisting of His-His-Pro-His-Gly (SEQ ID NO:8), His-Pro-Pro-His-Gly (SEQ ID NO:9), and Pro-Pro-Pro-His-Gly (SEQ ID NO:10); or

(ii) said addition variant ~~of said pentapeptide~~ wherein 1 to 4 amino acids selected from His, Pro and Gly are added at the N- or C- terminus of SEQ ID NO:8, SEQ ID NO:9 or SEQ ID NO:10.

3. *(withdrawn; **currently amended**):* A chemically synthesized peptide multimer comprising the pentapeptide or addition variant of claim 1, which multimer is selected from the group consisting of:

(a) a multimer having the formula $\mathbf{P^1}_n$ wherein

(i) $\mathbf{P^1}$ is the pentapeptide or addition variant of claim 1, and

(ii) **n**=2-8,

(b) a multimer having the formula $(\mathbf{P^1}\text{-}\mathbf{X}_m)_n\text{-}\mathbf{P^2}$, wherein

(i) $\mathbf{P^1}$ and $\mathbf{P^2}$ are said pentapeptides or addition variants according to claim 1,

(ii) $\mathbf{P^1}$ and $\mathbf{P^2}$ are the same or different ~~peptides~~;

(iii) **X** is C_1-C_5 alkyl, C_1-C_5 alkenyl, C_1-C_5 alkynyl, C_1-C_5 polyether containing up to 4 oxygen atoms;

(iv) **m** = 0 or 1; and

(v) **n** = 1-7,

and wherein the peptide multimer has substantially the same ligand binding activity or biological activity as [[of]] (1) human HPRG, (2) rabbit HPRG, or (3) a polypeptide domain of human or rabbit HPRG which is SEQ ID NO:5 or SEQ ID NO:6, and which biological activity is that of inhibiting angiogenesis, endothelial cell proliferation or endothelial tube formation in an *in vitro* or *in vivo* bioassay.

4. *(withdrawn **currently amended**):* A recombinantly produced peptide multimer comprising the pentapeptide or addition variant of claim 1, which multimer has the formula $(\mathbf{P^1}\text{-}\mathbf{Gly}_z)_n\text{-}\mathbf{P^2}$, wherein:

(i) $\mathbf{P^1}$ and $\mathbf{P^2}$ are the pentapeptides or addition variants according to claim 1,

(ii) $\mathbf{P^1}$ and $\mathbf{P^2}$ are the same or different;

(iii) z = 0-6; and

(iv) n = 1-100,

and wherein the peptide multimer has substantially the same ligand binding activity or biological activity as [[of]] (1) human HPRG, (2) rabbit HPRG, or (3) a polypeptide domain of human or rabbit HPRG which is SEQ ID NO:5 or SEQ ID NO:6, and which biological activity is that of inhibiting angiogenesis, endothelial cell proliferation or endothelial tube formation in an *in vitro* or *in vivo* bioassay.

5. *(currently amended)* A diagnostically or therapeutically labeled anti-angiogenic ~~polypeptide,~~ pentapeptide or addition variant according to claim 1 or 2.

Claim 6 (Cancelled).

6 ~~7~~. *(currently amended)* A diagnostically useful HPRG-related composition comprising:

(a) the diagnostically labeled ~~polypeptide or~~ pentapeptide or addition variant of claim 5; and

(b) a ~~diagnostically~~ pharmaceutically acceptable carrier.

7 ~~8~~. *(previously presented)* The diagnostically useful composition of claim 6 ~~7~~ wherein polypeptide or peptide is labeled with a detectable label is selected from the group consisting of a radionuclide, a PET-imageable agent, an MRI-imageable agent, a fluorescer, a fluorogen, a chromophore, a chromogen, a phosphorescer, a chemiluminescer or a bioluminescer.

8 ~~9~~. *(previously presented)* The diagnostically useful composition of claim 7 ~~8~~, wherein the detectable label is a radionuclide selected from the group consisting of ^{3}H, ^{14}C, ^{35}S, ^{67}Ga, ^{68}Ga, ^{72}As, ^{89}Zr, ^{97}Ru, ^{99}Tc, ^{111}In, ^{123}I, ^{125}I, ^{131}I, ^{169}Yb and ^{201}Tl.

9 ~~10~~. *(currently amended)* The diagnostically useful composition of claim[[s]] 7 ~~8~~ wherein the detectable label is a fluorescer or fluorogen selected from the group consisting of fluorescein, rhodamine, dansyl, phycoerythrin, phycocyanin, allophycocyanin, *o*-phthaldehyde, fluorescamine, a fluorescein derivative, Oregon Green, Rhodamine Green, Rhodol Green and Texas Red.

10 ~~11~~. *(currently amended)* : An anti-angiogenic pharmaceutical composition comprising:

(a) the ~~polypeptide or~~ pentapeptide or addition variant of claim 1 or 2; and

(b) a pharmaceutically acceptable carrier.

11 ~~12~~. *(currently amended)*: A therapeutic anti-angiogenic pharmaceutical composition comprising:

(a) the therapeutically labeled ~~polypeptide or~~ pentapeptide or addition variant of claim ~~5 to which is bound directly or indirectly a therapeutically active moiety~~; and

(b) a pharmaceutically acceptable carrier.

12 13. *(previously presented)* The pharmaceutical composition of claim 11 [[or 12]] in a form suitable for injection.

13 14. *(original)* The therapeutic pharmaceutical composition of claim 12 wherein the therapeutically active moiety is a radionuclide.

14 15. *(original)* The therapeutic pharmaceutical composition of claim 14, wherein the radionuclide is selected from the group consisting of ^{47}Sc, ^{67}Cu, ^{90}Y, ^{109}Pd, ^{125}I, ^{131}I, ^{186}Re, ^{188}Re, ^{199}Au, ^{211}At, ^{212}Pb and ^{217}Bi.

Claims 16 to 22 CANCELLED

15 23. *(withdrawn; currently amended):* A method for inhibiting cell migration, cell invasion, cell proliferation or angiogenesis, or for inducing apoptosis, comprising contacting cells associated with undesired cell migration, invasion, proliferation or angiogenesis with an effective amount of a ~~therapeutic~~ pharmaceutical composition according to claim 11.

16 24. *(withdrawn):* A method for treating a subject having a disease or condition associated with undesired cell migration, invasion, proliferation, or angiogenesis, comprising administering to the subject an effective amount of a pharmaceutical composition according to claim 11.

Claims 25 to 48 CANCELLED

17 49. *(currently amended):* An affinity ligand useful for binding to or isolating an HPRG-binding molecule or cells expressing [[the]] an HPRG-binding molecule, comprising a ~~polypeptide or~~ pentapeptide or addition variant according to claim 1 or 2, immobilized to a solid support or carrier.

18 50. *(withdrawn; currently amended):* A method for isolating a HPRG-binding molecule from a complex mixture comprising:

(a) contacting the mixture with the affinity ligand of claim 49;

(b) allowing any material in the mixture to bind to the ligand;

(c) removing unbound material from the ligand; and

(d) eluting the bound HPRG-binding molecule or cells.

19 ~~51~~. *(withdrawn; currently amended):* A method for isolating or enriching from a cell mixture cells expressing a HPRG-binding site or receptor ~~from a cell mixture~~, comprising:

(a) contacting the cell mixture with the affinity ligand of claim 17 ~~49~~;

(b) allowing any cells expressing the binding site or receptor to bind to the affinity ligand;

(c) separating cells bound to the affinity ligand ~~compound~~ from unbound cells; and

(d) removing the bound cells,

thereby isolating or enriching the HPRG binding site-expressing cells.

20 ~~52~~. *(withdrawn):* A diagnostically or therapeutically labeled peptide multimer according to claim 3 or 4.

21 ~~53~~. *(withdrawn):* An anti-angiogenic pharmaceutical composition comprising

(a) the peptide multimer of claim 3 or 4; and

(b) a pharmaceutically acceptable carrier.

22 ~~54~~. *(withdrawn; **currently amended**):* A therapeutic anti-angiogenic pharmaceutical composition according to claim 21 ~~53~~, wherein ~~comprising~~

~~(a) the peptide multimer of claim 3 or 4 to which~~ a therapeutically active moiety is bound directly or indirectly to the peptide multimer ~~a therapeutically active moiety; and~~

~~(b) a pharmaceutically acceptable carrier~~.

23 ~~55~~. *(withdrawn; currently amended):* An affinity ligand useful for binding to or isolating an HPRG-binding molecule or cells expressing [[the]] an HPRG-binding molecule, comprising a peptide multimer according to claim 3 or 4, immobilized to a solid support or carrier.

Claims 56-57 (Cancelled).

24 ~~58~~. *(new)* The pharmaceutical composition of claim 11 ~~12~~ in a form suitable for injection.

25 ~~59~~. *(new):* A method for inhibiting cell migration, cell invasion, cell proliferation or angiogenesis, or for inducing apoptosis, comprising contacting cells associated with undesired cell migration, invasion, proliferation or angiogenesis with an effective amount of a pharmaceutical composition according to claim 21 ~~53~~.

26 ~~60~~. *(new):* A method for treating a subject having a disease or condition associated with undesired cell migration, invasion, proliferation, or angiogenesis, comprising administering to the subject an effective amount of a pharmaceutical composition according to claim 21 ~~53~~.

27 ~~61~~. *(new):* A method for isolating a HPRG-binding molecule from a complex mixture comprising:

(a) contacting the mixture with the affinity ligand of claim 23 ~~55~~;

(b) allowing any material in the mixture to bind to the ligand;

(c) removing unbound material from the ligand; and

(d) eluting the bound HPRG-binding molecule or cells.

28 ~~62~~. *(new):* A method for isolating or enriching from a cell mixture cells expressing a HPRG-binding site or receptor, comprising:

(a) contacting the cell mixture with the affinity ligand of claim 23 ~~55~~;

(b) allowing any cells expressing the binding site or receptor to bind to the affinity ligand;

(c) separating cells bound to the affinity ligand from unbound cells; and

(d) removing the bound cells,

thereby isolating or enriching the HPRG binding site-expressing cells.

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PATENT

FORM PTO-1449 (Modified)
LIST OF PATENTS AND PUBLICATIONS
FOR APPLICANT'S INFORMATION DISCLOSURE STATEMENT
(Use several sheets if necessary)
Sheet 1 of 1

In the application of:
Fernando DONATE et al.
U.S. Application Serial No.: 10/074,225
Filing Date: February 14, 2002

For: HISTIDINE PROLINE RICH GLYCOPROTEIN (HPTG) AS AN ANTI-ANGIOGENIC AND ANTI-TUMOR AGENT

Examiner: Unassigned
Group Art Unit: 1636

U.S. PATENT DOCUMENTS

Ref #	Examiner's Initials	Document Number	Date	Name	(If appropriate) Filing Date

FOREIGN PATENT DOCUMENTS

Ref #	Examiner's Initials	Document Number	Date	Country	If appropriate) Filing Date
1.	DB	WO 01/62968A2	8/30/01	WIPO	
2.	DB	WO 91/06356A1	5/16/91	WIPO	

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, etc.)

Ref #	Examiner's Initials	
3.	DB	Koide et al., "Amino Acid sequence of Human Histidine-Rich Glycoprotein Derived from the Nucleotide Sequence...", April 1986, Vol. 25, No. 8, pages 2220-2225
4.		~~Borza D-B. et al., "Domain Structure And Conformation of Histidine-Proline-Rich Glycoprotein", Biochemistry, 1996, 35; 1925-1934)~~
5.		Hulett et al., "Murine histidine-rich glycoprotein: Cloning, characterization and cellular origin. Immunology and Cell Biology, 2000, Vol. 78, pages 280-287
6.	DB	Hennis et al., "Evidence for the Absence of Intron H of the Histidine-Rich Glycoprotein (HRG) Gene: Genetic Mapping and in Situ Localization of HRG to Chromosome 3q28-q29. Genomics, 1994, Vol. 19, pages 2195-197

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